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STRAUB & POKOTYLO
788 Shrewsbury Avenue
TINTON FALLS, NJ 07724

EXAMINER	
CROW, ROBERT THOMAS	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/768,977	ARNOLD ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *03 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33 and 40-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 3 January 2011 in which the specification and claims 1, 5-7, 14, and 18-20 were amended, no claims were canceled, and new claims 40-41 were added. All of the amendments have been thoroughly reviewed and entered.

The objections to the claims listed in the previous Office Action are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

The previous rejections under the judicially created doctrine of obviousness-type double patenting not reiterated below are withdrawn in view of Applicant's amendments to the instant claims and/or the amendments to the conflicting claims. However, new rejections necessitated by the amendments are presented below.

2. Claims 1-33 and 40-41 are under prosecution.

Claim Interpretation

3. As previously noted, claims 14-33 are drawn to a "system." The specification teaches a "system" wherein the "system" is defined in terms of **structural** limitations (e.g., pages 5 and 7-8 and Figure 1). In addition, claims 14-33 recite **structural** limitations of the "system." Thus, the "system" is interpreted to encompass any collection of reagents and parts used together that are not necessarily part of a completely integrated single unitary device. Any further interpretation of the word is considered an "intended use" and does not impart any further structural limitation on the claimed subject matter.

4. It is noted that the preamble be independent claim 1 reads "For use in a system including a light source, and a light detector, for measuring a target substance including a chain of nucleotides, a sensor comprising…." The terms "for use" and "for measuring" clearly indicated that the light source, and detector are not required of the claimed sensor. The courts have held that "while features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function." *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). In addition, "[A]pparatus claims cover what a device *is*, not what a device *does*." *Hewlett-Packard Co. v. Bausch &Lomb Inc.*, 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed. Cir. 1990) (emphasis in original). Therefore, the various uses recited in the preamble to the claim (e.g., all the text of the preamble preceding the phrase "a sensor comprising") fail to define

additional structural elements of the claimed sensor. Thus, only those structural limitations appearing after the phrase "a sensor comprising" are required by the claim. See MPEP § 2114.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 14-16, 21-22, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001).

Regarding claim 14, Maleki et al teach a system comprising a light source and a light detector in the form of an optical detection module (Figure 2). The system further comprises a sensor comprising an optical carrier in the form of a support having a chamber (paragraph 0035). The sensor further comprises two or more optical cavities in the form of multiple WGM (i.e., whisper gallery mode) cavities that form a detector array (paragraph 0048). The optical cavities are optically coupled to the optical carrier because signals from the WGM are optically detected (Figure 2). The detector is an optical detector (paragraph 0030), and thus detects light. The exterior surface of the WGM (i.e., optical) cavity is coated with a reactive surface in the form of a DNA molecule (i.e., an oligonucleotide; paragraph 0045). Because each WGM (i.e., optical)

cavity is coated with a different reactive surface for a different analyte (i.e., a different DNA oligonucleotide for a different DNA analyte; paragraphs 0048 and 0045), each of the optical cavities has a surface having an oligonucleotide complementary to one of the at least two target substances. Application of light causes resonance within each of the optical cavities (paragraph 0006). Maleki et al also teach the system comprise a processor for determining a measurement of the target substance using a difference in shifts between the resonances detected; namely, the system comprises a signal processing module (Figure 2 and paragraph 0031), wherein a difference between signal from the resonator in the absence of sample and the signal in the presence of the sample is processed to determine the property of the sample.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not posses characteristic relied on" (205 USPQ 594, second column, first full paragraph). While Maleki et al do not explicitly teach hybridization of the target substance to oligonucleotides shifts the resonance (which is detected to determine a measurement of the target substance), Maleki et al teach the analogous process of binding an antigen to an immobilized antibody causes a shift in the resonance, which is detected (paragraph 0046). Thus, the sensor of Maleki et al exhibits the same behavior when nucleic acid interactions are used instead of antibody/antigen interactions.

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in the claim (e.g., hybridizing a target substance and measuring the resonance shift) fail to define additional structural elements of the claimed sensor. Because Maleki et al teach all of the required structural limitations of the claimed system, the claim is anticipated by Maleki et al.

Regarding claim 15, Maleki et al teach the system of claim 14, wherein the optical carrier is an optical fiber (paragraph 0032).

Regarding claim 16, Maleki et al teach the system of claim 14, wherein at least one of the optical cavities is a microsphere; namely, the WGM is microsphere (Figure 1 and paragraph 0008).

Regarding claims 21-22, the system of claim 14 is discussed above. As noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in the claim (e.g., causing a shift upon target binding) refer to a use of the system and thus fail to define additional structural elements of the claimed system. Because Maleki et al teach all of the required structural limitations of the claimed system, the claim is anticipated by Maleki et al.

In addition, it is reiterated that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to prove that subject matter shown to be in the prior art does not posses characteristic relied on. While Maleki et al do not explicitly teach a ten-fold shift (i.e.,

claim 22) for single nucleotide mismatches (i.e., claim 21), it is believed that this is an inherent property of the claimed system.

Regarding claim 31, Maleki et al teach the system of claim 14, wherein the optical carrier includes a plurality of optical carriers; namely, the system comprises two optical fibers (paragraph 0032 and Figure 3A).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-3 and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Wang et al (Science, vol. 280, pages 1077-1082, 15 May 1998).

This is a new rejection necessitated by the amendments.

Regarding claim 1, Maleki et al teach a sensor comprising an optical carrier in the form of an optical fiber (paragraph 0032). The sensor further comprises two or more optical cavities in the form of multiple WGM (i.e., whisper gallery mode) cavities that form a detector array (paragraph 0048). The optical cavities are optically coupled to the optical carrier because signals from the WGM are optically detected (Figure 3). The exterior surface of the WGM (i.e., optical) cavity is coated with a reactive surface in the form of a DNA molecule (i.e., an oligonucleotide; paragraph 0045). Because each WGM (i.e., optical) cavity is coated with a different reactive surface for a different analyte (i.e., a different DNA oligonucleotide for a different DNA analyte; paragraphs 0048 and 0045), each of the optical cavities has a surface having an oligonucleotide complementary to one of the at least two target substances. Application of light causes resonance within each of the optical cavities (paragraph 0006).

As noted above, *In re Best* and *In re Fitzgerald* discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to prove that subject matter shown to be in the prior art does not posses characteristic relied on. While Maleki et al do not explicitly teach hybridization of the target substance to oligonucleotides shifts the

resonance (which is detected to determine a measurement of the target substance), Maleki et al teach the analogous process of binding an antigen to an immobilized antibody causes a shift in the resonance, which is detected (paragraph 0046). Thus, the system of Maleki et al exhibits the same behavior when nucleic acid interactions are used instead of antibody/antigen interactions.

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in the claim (e.g., hybridizing a target substance and measuring the resonance shift) fail to define additional structural elements of the claimed sensor. Because the prior art teaches all of the required structural limitations of the claimed sensor, the claim is obvious.

Maleki et al do not teach the first and second optical cavities comprise oligonucleotides for a target and a single nucleotide mismatch of the target.

However, Wang et al teach a sensor in the form of a DNA chip having multiple locations each having a different oligonucleotide thereon, wherein each probe has a different nucleotide in an identical position (page 1078, column 2). Thus, one probe is perfectly complementary to the target, and the other three probes each have a single mismatch with the target. Wang et al also teach the use of the mismatch probes in conjunction with the fully complementary probe has the added advantage of being useful in studying loss of heterozygosity in tumors and in association analysis of patients and controls (page 1077). Thus, Wang et al teach the known technique of providing a sensor having oligonucleotides for both a target and for a single nucleotide mismatch of the target.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the sensor comprising two different oligonucleotides in each optical cavity as taught by Maleki et al so that the oligonucleotides are for both a target and for a single nucleotide mismatch of the target in accordance with the teachings of Wang et al to arrive at the instantly claimed sensor with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a sensor having the added advantage of being useful in studying loss of heterozygosity in tumors and in association analysis of patients and controls as explicitly taught by Wang et al (page 1077). In addition, it would have been obvious to the ordinary artisan that the known technique of providing a sensor having oligonucleotides for both a target and for a single nucleotide mismatch of the target as taught by Wang et al could have been applied to the sensor of Maleki et al with predictable results because the known technique of providing a sensor having oligonucleotides for both a target and for a single nucleotide mismatch of the target as taught by Wang et al results in oligonucleotides useful in the study of genetic diseases.

Regarding claim 2, the sensor of claim 1 is discussed above. Maleki et al teach the optical carrier is an optical fiber (paragraph 0032).

Regarding claim 3, the sensor of claim 1 is discussed above. Maleki et al also teach at least one of the optical cavities is a microsphere; namely, the WGM is microsphere (Figures 1-2 and paragraph 0008).

Regarding claim 6, the sensor of claim 1 is discussed above. Wang et al teach the first oligonucleotide is complementary to a target DNA (page 1078). Thus, modification of the sensor of Maleki et al with the teachings of Wang et al results in a sensor wherein the first oligonucleotide is complementary to a target DNA.

Regarding claim 7, the device of claim 1 is discussed above.

It is reiterated that *In re Best* and *In re Fitzgerald* discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to prove that subject matter shown to be in the prior art does not posses characteristic relied on. Wang et al teach the use of common variants in gene coding regions (page 1079). The sequences of the coding regions are present in mRNA produced from the genes. Therefore, the first oligonucleotides, which are complementary to the gene coding region targets, are also complementary to mRNA targets.

Regarding claims 8-9, the device of claim 1 is discussed above. As noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in the claim (e.g., causing a shift upon target binding) refer to a use of the sensor and thus fail to define additional structural elements of the claimed sensor. Because the prior art teaches all of the required structural limitations of the claimed sensor, the claim is obvious.

In addition, it is reiterated that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject

matter which there is reason to believe includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to prove that subject matter shown to be in the prior art does not posses characteristic relied on. While Maleki et al do not explicitly teach a ten-fold shift I.e., claim 9) for single nucleotide mismatches (i.e., claim 8), it is believed that this is an inherent property of the claimed sensor.

10. Claims 4-5 and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Wang et al (Science, vol. 280, pages 1077-1082, 15 May 1998) as applied to claim 1 above, and further in view of Boyd et al (U.S. Patent Application Publication No. US 2004/0023396 A1, filed 14 November 2002).

This is a new rejection necessitated by the amendments.

Regarding claims 4-5 and 10-13, the sensor of claim 1 is discussed above in Section 9.

While Maleki et al teaches disks (paragraph 0016), neither Maleki et al nor Wang et al specifically teach toroidal microcavities, indium phosphide (i.e., InP) microdisks or the lengths of the nucleic acids.

However, Boyd et al teach a sensor comprising optical carrier 14 and an optical cavity in the form of a resonator 20 (Figure 1A). The sensor has multiple resonators (i.e., optical cavities) on the carrier (i.e., waveguide; paragraph 0046). Each resonator surface has different oligonucleotide probes thereon (i.e., for different target nucleotide

chain analytes; paragraphs 0030-0033). Light is applied to the carrier, and a shift (i.e., change) in resonance is detected (Abstract). Boyd et al also teach the optical cavity is either a toroidal (i.e., ring-shaped) microcavity (i.e., claim 4, Abstract), or a microdisk (Abstract), wherein the microdisk in an InP microdisk (i.e., claim 5; paragraph 0022).

Boyd et al further teach the length of the oligonucleotide is at least about 7 nucleotides up to about 100 nucleotides in length (paragraph 0033), which encompasses the claimed value of 11 nucleotides (i.e., claims 10 and 12) and 27 nucleotides (i.e., claims 11 and 13).

Boyd et al teach the sensor has the added advantage of readily identifying minute quantities of biological targets (paragraph 0006). Thus, Boyd et al teach the known technique of using toroidal microcavities, indium phosphide (i.e., InP) microdisks, and the claimed lengths of the nucleic acids.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the sensor as taught by Maleki et al in view of Wang et al to comprise the toroidal microcavities, indium phosphide (i.e., InP) microdisks, and the claimed lengths of the nucleic acids in accordance with the teachings of Boyd et al to arrive at the instantly claimed sensor with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a sensor having the added advantage of readily identifying minute quantities of biological targets as explicitly taught by Boyd et al (paragraph 0006). In addition, it would have been obvious to the ordinary artisan that the known technique of using toroidal microcavities, indium

phosphide (i.e., InP) microdisks, and the claimed lengths of the nucleic acids taught by Boyd et al could have been applied to the sensor of Maleki et al in view of Wang et al with predictable results because the known technique of using toroidal microcavities, indium phosphide (i.e., InP) microdisks, and the claimed lengths of the nucleic acids taught by Boyd et al predictably results in a sensor useful for nucleic acid assays.

11. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Wang et al (Science, vol. 280, pages 1077-1082, 15 May 1998) as applied to claim 1 above, and further in view of Serafini et al (U.S. Patent No. 6,110,711, issued 29 August 2000).

This is a new rejection necessitated by the amendments.

It is noted that while claim 7 has been rejected under 35 U.S.C 103(a) as described above in Section 9, the claim is also obvious using the interpretation outlined below.

Regarding claim 7, the sensor of claim 1 is discussed above in Section 9.

Neither Maleki et al nor Wang et al explicitly teach the target is RNA.

However, Serafini et al teach the detection of mRNA has the added advantage of allowing measurement of gene expression in a cell, thus defining the type of cell (Abstract). Thus, Serafini et al teach the known technique of using RNA as a target.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the sensor as taught by Maleki et

al in view of Wang et al to so that the oligonucleotides are complementary to RNA targets in accordance with the teachings of Serafini et al to arrive at the instantly claimed sensor with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a sensor having the added advantage of allowing measurement of gene expression in a cell, thus defining the type of cell as explicitly taught by Serafini et al (Abstract). In addition, it would have been obvious to the ordinary artisan that the known technique of using RNA targets as taught by Serafini et al could have been applied to the sensor of Maleki et al in view of Wang et al with predictable results because the known technique of using RNA targets as taught by Serafini et al predictably results in a sensor useful for genetic assays.

12. Claims 14, 17-18, 23-27, 31, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) as applied to claim 14 above, and further in view of Boyd et al (U.S. Patent Application Publication No. US 2004/0023396 A1, filed 14 November 2002).

This is a new rejection necessitated by the amendments.

It is noted that this rejection applies to claims 14 and 31 to the extent that they are drawn to the embodiments of dependent claims 17-18, 23-27, and 33.

Regarding claims 17-18, 23-27, and 33, Maleki et al teach the system of claim 14, which comprises a light source and a light detector in the form of an optical

detection module (Figure 2). The system further comprises a sensor comprising an optical carrier in the form of a support having a chamber (paragraph 0035). The sensor further comprises two or more optical cavities in the form of multiple WGM (i.e., whisper gallery mode) cavities that form a detector array (paragraph 0048). The optical cavities are optically coupled to the optical carrier because signals from the WGM are optically detected (Figure 2). The detector is an optical detector (paragraph 0030), and thus detects light. The exterior surface of the WGM (i.e., optical) cavity is coated with a reactive surface in the form of a DNA molecule (i.e., an oligonucleotide; paragraph 0045). Because each WGM (i.e., optical) cavity is coated with a different reactive surface for a different analyte (i.e., a different DNA oligonucleotide for a different DNA analyte; paragraphs 0048 and 0045), each of the optical cavities has a surface having an oligonucleotide complementary to one of the at least two target substances. Application of light causes resonance within each of the optical cavities (paragraph 0006). Maleki et al also teach the system comprise a processor for determining a measurement of the target substance using a difference in shifts between the resonances detected; namely, the system comprises a signal processing module (Figure 2 and paragraph 0031), wherein a difference between signal from the resonator in the absence of sample and the signal in the presence of the sample is processed to determine the property of the sample.

It is reiterated that *In re Best* and *In re Fitzgerald* discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe includes functions that are newly cited or is identical to a product instantly claimed. In

such a situation the burden is shifted to the applicants to prove that subject matter shown to be in the prior art does not posses characteristic relied on. While Maleki et al do not explicitly teach hybridization of the target substance to oligonucleotides shifts the resonance (which is detected to determine a measurement of the target substance), Maleki et al teach the analogous process of binding an antigen to an immobilized antibody causes a shift in the resonance, which is detected (paragraph 0046). Thus, the sensor of Maleki et al exhibits the same behavior when nucleic acid interactions are used instead of antibody/antigen interactions.

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in the claim (e.g., hybridizing a target substance and measuring the resonance shift) fail to define additional structural elements of the claimed sensor. Because the prior art teaches all of the required structural limitations of the claimed sensor, the claim is obvious.

Maleki et al also teach the system of claim 31, wherein the optical carrier includes a plurality of optical carriers; namely, the system comprises two optical fibers (paragraph 0032 and Figure 3A).

While Maleki et al teaches disks (paragraph 0016) and while Maleki et al teach optical fibers (paragraph 0032 and Figure 3A), neither Maleki et al nor Wang et al specifically teach toroidal microcavities (i.e., claim 17), indium phosphide (i.e., InP) microdisks (i.e., claim 18), the claimed lengths of the nucleic acids (i.e., claims 23-26), refractive indices (i.e., claim 27), or multiple detectors (i.e., claim 33).

However, Boyd et al teach a sensor system comprising optical carrier 14 and an optical cavity in the form of a resonator 20 (Figure 1A). The sensor has multiple resonators (i.e., optical cavities) on the carrier (i.e., waveguide; paragraph 0046). Each resonator surface has different oligonucleotide probes thereon (i.e., for different target nucleotide chain analytes; paragraphs 0030-0033). Light is applied to the carrier, and a shift (i.e., change) in resonance is detected (Abstract). Boyd et al also teach the optical cavity is either a toroidal (i.e., ring-shaped) microcavity (i.e., claim 17, Abstract), or a microdisk (Abstract), wherein the microdisk in an InP microdisk (i.e., claim 18; paragraph 0022).

Boyd et al further teach the length of the oligonucleotide is at least about 7 nucleotides up to about 100 nucleotides in length (paragraph 0033), which encompasses the claimed value of 11 nucleotides (i.e., claims 23 and 25) and 27 nucleotides (i.e., claims 24 and 26).

Boyd et al further teach a system wherein the processor (i.e., monitoring system) determines the combination of a shift in characteristic of the resonance detected and the effective refractive index of the resonator (i.e., claim 27; paragraphs 0044 and 0046).

As noted above, and *In re Fitzgerald* discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to prove that subject matter shown to be in the prior art does not posses characteristic relied on. While Boyd et al do not explicitly the

change in refractive index is of a solution and the optical cavity, the processor does measure the effective refractive index of the resonator as discussed above. Thus, when the resonator is contacted with a solution of the target substance, the processor is capable of performing the claimed function.

In addition, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in the claim (e.g., measure a change in the refractive index upon addition of the solution) refer to a use of the system, and thus fail to define additional structural elements of the claimed system. Because the prior art teaches all of the required structural limitations of the claimed system, the claim is obvious.

Boyd et al also teach the system wherein there are at least two detectors, one light source, and two fibers are coupled to the light source but are coupled to different detectors (i.e., claim 33; Figure 1C).

Boyd et al teach the sensor has the added advantage of readily identifying minute quantities of biological targets (paragraph 0006). Thus, Boyd et al teach the known technique of providing the limitations of the instant claims.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the system as taught by Maleki et al to comprise the claimed limitations in accordance with the teachings of Boyd et al to arrive at the instantly claimed system with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a system having the added advantage of readily

identifying minute quantities of biological targets as explicitly taught by Boyd et al (paragraph 0006). In addition, it would have been obvious to the ordinary artisan that the known technique of using the claimed limitations as taught by Boyd et al could have been applied to the system of Maleki et al with predictable results because the known technique of using the claimed limitations as by Boyd et al predictably results in a system useful for nucleic acid assays.

13. Claims 14 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Wang et al (Science, vol. 280, pages 1077-1082, 15 May 1998).

This is a new rejection necessitated by the amendments.

It is noted that this rejection applies to claim 14 to the extent that it is drawn to the embodiments of dependent claims 19-20.

Regarding claims 19-20, the system of claim 14 is discussed above in Sections 6 and 12.

Maleki et al do not teach explicitly teach the oligonucleotides are complementary to targets that are DNA or RNA.

However, Wang et al teach a sensor system in the form of a DNA chip having multiple locations each having a different oligonucleotide thereon, wherein the oligonucleotides are complementary to genomic DNA (page 1078, column 2).

It is reiterated that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter

which there is reason to believe includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to prove that subject matter shown to be in the prior art does not posses characteristic relied on. Wang et al teach the use of common variants in gene coding regions (page 1079). The sequences of the coding regions are present in mRNA produced from the genes. Therefore, the first oligonucleotides, which are complementary to the gene coding region targets, are also complementary to mRNA targets.

Wang et al also teach the use of the probes has the added advantage of being useful in studying loss of heterozygosity in tumors and in association analysis of patients and controls (page 1077). Thus, Wang et al teach the known technique of providing a system having oligonucleotides for both DNA and RNA targets.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the system comprising two different oligonucleotides in each optical cavity as taught by Maleki et al so that the oligonucleotides are for both DNA or RNA targets in accordance with the teachings of Wang et al to arrive at the instantly claimed system with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a system having the added advantage of being useful in studying loss of heterozygosity in tumors and in association analysis of patients and controls as explicitly taught by Wang et al (page 1077). In addition, it would have been obvious to the ordinary artisan that the known technique of providing a sensor having oligonucleotides for both RNA and DNA targets as taught by Wang et al

could have been applied to the system of Maleki et al with predictable results because the known technique of providing a system having oligonucleotides for both DNA and RNA targets as taught by Wang et al results in oligonucleotides useful in the study of genetic diseases.

14. Claims 14 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Serafini et al (U.S. Patent No. 6,110,711, issued 29 August 2000).

This is a new rejection necessitated by the amendments.

It is noted that this rejection applies to claim 14 to the extent that it is drawn to the embodiment of dependent claim 20.

It is noted that while claim 20 has been rejected under 35 U.S.C 103(a) as described above in Section 13, the claim is also obvious using the interpretation outlined below.

Regarding claim 20, the system of claim 14 is discussed above in Sections 6 and 12.

Maleki et al do not teach explicitly teach the oligonucleotides are complementary to targets that are RNA.

However, Serafini et al teach the detection of mRNA has the added advantage of allowing measurement of gene expression in a cell, thus defining the type of cell (Abstract). Thus, Serafini et al teach the known technique of using RNA as a target.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the system as taught by Maleki et al so that the oligonucleotides are complementary to RNA targets in accordance with the teachings of Serafini et al to arrive at the instantly claimed system with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a system having the added advantage of allowing measurement of gene expression in a cell, thus defining the type of cell as explicitly taught by Serafini et al (Abstract). In addition, it would have been obvious to the ordinary artisan that the known technique of using RNA targets as taught by Serafini et al could have been applied to the system of Maleki et al with predictable results because the known technique of using RNA targets as taught by Serafini et al predictably results in a system useful for genetic assays.

15. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Boyd et al (U.S. Patent Application Publication No. US 2004/0023396 A1, filed 14 November 2002) as applied to claim 27 above, and further in view of Vollmer et al (Appl. Phys. Lett., vol. 80, pages 4057-4059 (2002)).

This is a new rejection necessitated by the amendments.

Regarding claim 28, the system of claim 27 is discussed above in Section 12. Maleki et al teach the signal obtained from the analyte is compared to that of a control signal (paragraph 0007).

Neither Wang et al nor Maleki et al teach measurement of polarizability.

However, Vollmer et al teach a system comprising an optical (i.e., resonant) microcavity (Abstract). Vollmer et al also teach the calculation of surface density based on the excess polarizability and the radius (i.e., of a microsphere; page 4058, column 2). Vollmer et al also teach the calculation has the added advantage of verifying the surface density, which in turn established the smallest weight detectable by the system (pages 4058, column 2). Thus, Vollmer et al teach the known technique of measuring polarizability.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the processor in system of Maleki et al in view of Wang et al, which measures the analyte via comparison to a control (i.e., equal volume of solution) so that the processor performs the calculation of surface density based on polarizability in accordance with the teachings of Vollmer et al to arrive at the instantly claimed system with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a system having the added advantage of verifying the surface density, which in turn established the smallest weight detectable by the system, as explicitly taught by Vollmer et al (pages 4058, column 2). In addition, it would have been obvious to the ordinary artisan that the known technique of measuring polarizability) as taught by Vollmer et al could have been applied to the system of Maleki et al in view of Wang et al with predictable results because the known technique

of measuring polarizability as taught by Vollmer et al predictably results in calculation of useful data for the proper operation of a biosensor.

16. Claims 14 and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Vollmer et al (Appl. Phys. Lett., vol. 80, pages 4057-4059 (2002)).

This is a new rejection necessitated by the amendments.

It is noted that this rejection applies to claim 14 to the extent that it is drawn to the embodiments of dependent claims 29-30.

Regarding claims 28-30, the system of claim 14 is discussed above in Sections 6 and 12.

While Maleki et al teach the signal obtained from the analyte is compared to that of a control signal (paragraph 0007), neither Maleki et al nor Wang et al teach measurement of the radius of the microsphere (i.e., claim 29), or the surface density (i.e., claim 30).

However, Vollmer et al teach a system comprising an optical (i.e., resonant) microcavity (Abstract). Vollmer et al also teach the calculation of surface density based on the excess polarizability and the radius (i.e., of a microsphere; page 4058, column 2). Vollmer et al also teach the calculation has the added advantage of verifying the surface density, which in turn established the smallest weight detectable by the system

(pages 4058, column 2). Thus, Vollmer et al teach the known technique of measuring the radius of the microsphere (i.e., claim 29), and the surface density (i.e., claim 30).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the processor in system of Maleki et al in view of Wang et al , which measures the analyte via comparison to a control (i.e., equal volume of solution) so that the processor performs the calculation of surface density (i.e., claims 30) based on polarizability and the radius of the microsphere (i.e., claim 29) in accordance with the teachings of Vollmer et al to arrive at the instantly claimed system with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a system having the added advantage of verifying the surface density, which in turn established the smallest weight detectable by the system, as explicitly taught by Vollmer et al (pages 4058, column 2). In addition, it would have been obvious to the ordinary artisan that the known technique of measuring the radius of the microsphere (i.e., claim 29) and the surface density (i.e., claim 30) as taught by Vollmer et al could have been applied to the system of Maleki et al in view of Wang et al with predictable results because the known technique of measuring the radius of the microsphere and the surface density (i.e., claim 30) as taught by Vollmer et al predictably results in calculation of useful data for the proper operation of a biosensor.

17. Claims 14 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Hunziker et al (U.S. Patent No. 6,583,399 B1, issued 24 June 2003; filed 22 November 2000).

This is a new rejection necessitated by the amendments.

It is noted that this rejection applies to claims 14 and 31 to the extent that they are drawn to the embodiment of dependent claim 22.

Regarding claim 32, the system of claim 14 is discussed above in Sections 6 and 12.

Maleki et al also teach the system of claim 31, wherein the optical carrier includes a plurality of optical carriers; namely, the system comprises two optical fibers (paragraph 0032 and Figure 3A).

Maleki et al do not teach a plurality of optical fibers.

However, Hunziker et al teach a sensor comprising an optical carrier in the form of optical coupler 14, and at least two optical cavities in the form of optical resonators 16, wherein each of the optical fibers 14 is coupled with at least two optical cavities 16, which has the added advantage of allowing reach resonator to be monitored independently (Figure 2G and column 7, lines 1-30). Thus, Hunziker et al teach the known technique of providing a plurality of optical fibers.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the system of Maleki et al so that the system comprises a plurality of optical fibers optically coupled with the optical

cavities in accordance with the teachings of Hunziker et al to arrive at the instantly claimed system with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a system having the added advantage of allowing reach resonator to be monitored independently explicitly taught by Hunziker et al (Figure 2G and column 7, lines 1-30). In addition, it would have been obvious to the ordinary artisan that the known technique of providing a plurality of optical fibers taught by Hunziker et al could have been applied to the system of Maleki et al with predictable results because the known technique of providing a plurality of optical fibers taught by Hunziker et al predictably results in an arrangement useful for optical detection.

18. Claims 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (U.S. Patent Application Publication No. US 2002/0097401, filed 8 August 2001) in view of Wang et al (Science, vol. 280, pages 1077-1082, 15 May 1998) as applied to claim 1 above, and further in view of Vollmer et al (Appl. Phys. Lett., vol. 80, pages 4057-4059 (2002)).

This is a new rejection necessitated by the amendments.

Regarding claims 40-41, the sensor of claim 1 is discussed above in Section 9.

Neither Maleki et al nor Wang et al teach the parallel plates.

However, Vollmer et al teach an optical carrier (i.e., fiber) and an optical cavity (i.e., spheroid) placed between two parallel substrates (i.e., glass slides), which has the

added advantage of retaining the sample solution therein (page 4057 and Figure 1). Thus, Vollmer et al teach the known technique of providing parallel plates.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the sensor of Maleki et al in view of Wang et al so that the optical carriers and an optical cavities are placed between two parallel substrates in accordance with the teachings of Vollmer et al to arrive at the instantly claimed sensor with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a sensor having the added advantage of allowing retention of the sample solution therein explicitly taught by Vollmer et al (Figure 1 and page 4057). In addition, it would have been obvious to the ordinary artisan that the known technique of providing the parallel plates as taught by Vollmer et al could have been applied to the system of Maleki et al in view of Wang et al with predictable results because the known technique of providing the parallel plates as taught by Vollmer et al predictably results in an arrangement useful for optical detection.

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 1-3 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 8-22, and 26-28 of U.S. Patent No. 7,491,491 B2 in view of Wang et al (Science, vol. 280, pages 1077-1082, 15 May 1998).

This is a new rejection necessitated by the amendments.

The '491 claims describe the same limitations as the instant claims; namely, a sensor comprising an optical carrier (i.e., fiber), microspheres, immobilized oligonucleotides, and resonance shifts. For example, the limitations of instant claim 3 are met by claims 1-2 of the '491 patent. The additional limitations of the '491 claims are encompassed by the open claims language "comprising" found in the instant claims.

The ‘491 claims do not require the first and second optical cavities comprise oligonucleotides for a target and a single nucleotide mismatch of the target.

However, Wang et al teach a sensor in the form of a DNA chip having multiple locations each having a different oligonucleotide thereon, wherein each probe has a different nucleotide in an identical position (page 1078, column 2). Thus, one probe is perfectly complementary to the target, and the other three probes each have a single mismatch with the target. Wang et al also teach the use of the mismatch probes in conjunction with the fully complementary probe has the added advantage of being useful in studying loss of heterozygosity in tumors and in association analysis of patients and controls (page 1077). Thus, Wang et al teach the known technique of providing a sensor having oligonucleotides for both a target and for a single nucleotide mismatch of the target.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the sensor of the ‘491 claims to comprise oligonucleotides are for both a target and for a single nucleotide mismatch of the target in accordance with the teachings of Wang et al to arrive at the instantly claimed sensor with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a sensor having the added advantage of being useful in studying loss of heterozygosity in tumors and in association analysis of patients and controls as explicitly taught by Wang et al (page 1077). In addition, it would have been obvious to the ordinary artisan that the known technique of providing a sensor having

oligonucleotides for both a target and for a single nucleotide mismatch of the target as taught by Wang et al could have been applied to the sensor of the '491 claims with predictable results because the known technique of providing a sensor having oligonucleotides for both a target and for a single nucleotide mismatch of the target as taught by Wang et al results in oligonucleotides useful in the study of genetic diseases.

Response to Arguments

21. Applicant's arguments filed 3 January 2011 (hereafter the "Remarks") have been fully considered but they are not persuasive for the reasons discussed below.

A. Applicant's request for an interview of page 11 of the Remarks is noted. However, the period allowed for the examiner's reply to Applicant's amendments is prohibitive of an interview before of Office Action must be mailed. In the future, should Applicant desire an interview, Applicant is encouraged to request the interview before filing any response, so that there is adequate time for the interview before the case is due.

B. Applicant argues on page 4 of the Remarks that Maleki et al do not teach the processor uses a difference in shifts.

However, as noted above, Maleki et al do teach the system comprises a processor for determining a measurement of the target substance using a difference in shifts between the resonances detected; namely, the system comprises a signal processing module (Figure 2 and paragraph 0031), wherein a difference between signal

from the resonator in the absence of sample and the signal in the presence of the sample is processed to determine the property of the sample.

C. Applicant's remaining arguments with respect to the previous rejections of the claims have been considered, but are either moot in view of the new ground(s) of rejection necessitated by the amendments or rely on arguments set forth to address the rejections of the claims as anticipated by Maleki et al under 35 USC 102(b). These arguments are addressed above. Since the arguments regarding the teachings of the processor of Maleki et al were not persuasive, the claims remain rejected for the reasons discussed above.

Conclusion

22. No claim is allowed.

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

24. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Primary Examiner
Art Unit 1634

/Robert T. Crow/
Primary Examiner, Art Unit 1634